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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/769,831	02/02/2004	Nikolai Franz Gregor Schwabe	S-844-US	9233

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SIEBERTH & PATTY, LLC
4703 BLUEBONNET BLVD
BATON ROUGE, LA 70809

EXAMINER	
DIBRINO, MARIANNE NMN	
ART UNIT	PAPER NUMBER
1644	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/04/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/769,831	SCHWABE ET AL.	
	Examiner	Art Unit	
	DiBrino Marianne	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) *13-19 and 21-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12 and 20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/21/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's response filed 10/30/06 is acknowledged and has been entered.

2. Applicant's election with traverse of Group I (claims 1-12 and 20), and species of light detectable label in Applicant's said response is acknowledged.

The basis of Applicant's traversal is of record in the said response on pages 1-2.

Applicant's arguments have been fully considered but are not persuasive.

It is the Examiner's position that examination of all the Groups that share the same or overlapping classification would impose an undue burden on the Examiner because they require a different field of search. Where it is necessary to search for one of the inventions in a manner that is not likely to result in finding art pertinent to the other inventions (*e.g.,* searching different classes/subclasses or electronic resources, or employing different search queries, a different field of search is shown, even though the two are classifiable together. The indicated different field of search must in fact be pertinent to the type of subject matter covered by the claims. (see MPEP § 808.02). It is the Examiner's further position that payment of a fee for claims over 20 has no bearing on the requirement for restriction.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1, 2, 4-6, 7, 11, 12 and 20 read on the elected species.

Upon consideration of the prior art reference US 2005/0003431 A1 listed below in this Office Action, claims 2, 3 and 8-10 are included in examination.

Accordingly, claims 13-19 and 21-23 (non-elected groups 49-160) are withdrawn from further consideration by the Examiner, 37 CFR 1.142(b), as being drawn to non-elected inventions.

Claims 1-12 and 20 are currently being examined. Claims 4, 5 and 20 are being examined to the extent they read upon amino acid residues 20-83 of COMP.

3. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP 602.01 and 602.02.

The oath or declaration is defective because: A CIP application filed under 37 CFR 1.53(b) may not be filed with a copy of the oath or declaration from the prior nonprovisional application. See 37 CFR 1.63(d)(1)(iv).

4. Applicant's Figures 1 and 3 filed 2/2/04 and Applicant's Figure 2 filed 6/4/04 are acceptable.

5. Acknowledgment is made of Applicant's claim for foreign priority based on an application filed in UK on 8/21/02. It is noted, however, that Applicant has not filed a certified copy of the 0219459.8 application as required by 35 U.S.C. 119(b).

6. The disclosure is objected to because of the following informalities:

a. The first sentence of the specification at [0001] has blank underlined spaces.

b. The use of the trademarks CENTRICON and MINIKROS have been noted in this application at [0109] and [0112], respectively. They should be capitalized wherever they appear and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Appropriate correction(s) is/are required.

7. Applicant is required to amend the specification to list the appropriate SEQ ID NOS for sequences disclosed in the specification (for example, at [0115] for SEQ ID NO: 1). See 37 C.F.R. 1.821(d).

8. The incorporation of essential material in the specification by reference to an unpublished U.S. application, foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference, if the material is relied upon to overcome any objection, rejection, or other requirement imposed by the Office. The amendment must be accompanied by a statement executed by the applicant, or a practitioner representing the applicant, stating that the material being inserted is the material previously incorporated by reference and that the amendment contains no new matter. 37 CFR 1.57(f).

The attempt to incorporate subject matter into the instant application by reference to foreign patents and non-published foreign patent applications on page 45 is improper because an application as filed must be complete in itself in order to comply with 35 USC 112. An application for a patent when filed may incorporate "essential material" by reference to (1) a US patent or (2) a US patent application publication, which patent or patent publication does not itself incorporate such essential material by reference. "Essential material" is defined as that which is necessary to (1) provide a written description of the claimed invention, and the manner and process of making and using it, in such full, concise and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and set forth the best mode contemplated by the inventor of carrying out the invention, (2) describe the claimed invention in terms that particularly point out and distinctly claim the invention as required by the second paragraph of 35 USC 112, or (3) describe the structure, material or acts that correspond to a claimed means or step for performing a specified function as required by the sixth paragraph of 35 USC 112. In any application which is to issue as a US patent, essential material may not be incorporated by reference to (1) patents or applications published by foreign countries or a regional patent office, (2) non-patent publications, (3) a US patent or application which itself incorporates "essential material" by reference, or (4) a foreign application. See *In re Fouche*, 439 F.2d 1237, 169 USPQ 429 (CCPA 1971).

In the instant case, the specification at [0009] discloses "Self-assembly of the protein to form pentamers is achieved through the formation of a five-stranded helical bundle that involves 64 N-terminal amino acid residues of the protein. The amino acid sequence of the oligomerisation domain has been disclosed by Efimov *et al.*, FEBS Letters 341: 54-48 (1994)." The specification further discloses at [0118] "Each and every patent or other published document referred to in any portion of this specification is incorporated *in toto* into this disclosure by reference, as if fully set forth herein."

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:
> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 4-5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claim 4 is indefinite in the recitation of "wherein the oligomerising domain....is derived from the pentamerisation domain of...COMP" because it is not clear what is meant, *i.e.,* what portion of the oligomerising domain is retained and which portion is not with regard to "is derived from", and what the actual pentamerisation domain of COMP is given that the instant specification identifies that self assembly of the protein to form pentamers is achieved through the

formation of a five stranded helical bundle that involves some 64 N-terminal amino acid residues of the COMP protein and further discloses that the amino acid sequence of the oligomerisation domain has been disclosed by Efirmov *et al* which is incorporated by reference.

b. Claim 5 is indefinite in the recitation of "wherein the pentamerisation domain of COMP...comprise and preferably consists of the amino acids 1 to 128, preferably 20 to 83, most preferably 20-72 of COMP" because it is not clear what the metes and scope of the claim are, *i.e.,* which amino acid residues actually are meant. In addition, it is not clear what is meant by "pentamerisation domain" with regard to the amino acid residues recited in the instant claim because the Efirmov *et al* article incorporated by reference into the instant specification identifies the pentamerization domain of COMP as amino acid residues 20-83 (page 57, column 2, last paragraph of said article and abstract).

11. For the purpose of prior art rejections, the filing date of the instant claims is deemed to be the filing date of the instant application, *i.e.,* 2/2/04, as the parent applications have not been provided by Applicant.

12: The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

13. Claims 1-3, 6-12 and 20 are rejected under 35 U.S.C. 102(e) as being anticipated by US 2005/0003431 A1 (priority to at least 2/12/99).

US 2005/0003431 A1 discloses oligomeric, including divalent, tetravalent, pentavalent and decavalent, MHC class II or MHC class I complexes comprising the extracellular regions of either the MHC α or β chain, a linker, a coiled-coil dimerization domain such as leucine zippers, or wherein the said complexes comprise the said regions of MHC, a linker, IgM constant chain domains, a linker and coiled-coil dimierization domains, or wherein the said complexes may further comprise tag such as an antibody, a polyHis tag or streptavidin, biotin or a biotin ligase recognition tag and radioactive or fluorescent labels. US 2005/0003431 A1 discloses that the complexes may further comprise the complementary MHC α or β chain extracellular regions and antigenic peptide, such that functional MHC binding complexes are formed. US 2005/0003431 A1 discloses pharmaceutical and diagnostic compositions comprising the said complexes, and the advantageous increase in avidity of binding to T cells using MHC

oligomers/multimers versus monomers (especially claim 1, abstract, [0008]-[0085], [0019]-[[0124], [0147]-[0149], [0155]-[0161]).

Claim 20 is included in this rejection because it is an inherent property of the pharmaceutical composition taught by the art reference that it contains a pharmaceutically acceptable carrier.

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

15. Claims 1, 4, 5 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 2005/0003431 A1 in view of Terskikh *et al* (PNAS USA 1997, 94:1663-1668, IDS reference), Muller *et al* (Meth. Enzymol. 2000, 326, pages 261-282, IDS reference), Efimov *et al* (FEBS Letters, 1994, 341: 54-48) and Efimov *et al* (Proteins 1996, 24: 259-262).

US 2005/0003431 A1 discloses oligomeric, including divalent, tetravalent, pentavalent and decavalent, MHC class II or MHC class I complexes comprising the extracellular regions of either the MHC α or β chain, a linker, a coiled-coil dimerization domain such as leucine zippers, or wherein the said complexes comprise the said regions of MHC, a linker, IgM constant chain domains, a linker and coiled-coil dimierization domains, or wherein the said complexes may further comprise tag such as an antibody, a polyHis tag or streptavidin, biotin or a biotin ligase recognition tag and radioactive or fluorescent labels. US 2005/0003431 A1 discloses that the complexes may further comprise the complementary MHC α or β chain extracellular regions and antigenic peptide, such that functional MHC binding complexes are formed. US 2005/0003431 A1 discloses pharmaceutical and diagnostic compositions comprising the said complexes, and the advantageous increase in avidity of binding to T cells using MHC oligomers/multimers versus monomers (especially claim 1, abstract, [0008]-[0085], [0019]-[[0124], [0147]-[0149], [0155]-[0161]).

US 2005/0003431 A1 does not disclose an oligomeric MHC complex wherein the oligomerising domain is derived from an oligomer-forming coiled-coil protein that is COMP.

Terskikh *et al* teach a pentameric antibody complex comprising the pentamerization domain of COMP, a coiled-coil assembly domain. Terskikh *et al* teach that the COMP assembly domain spontaneously forms a five-stranded α helical bundle, the highest oligomerization state know for a compact coiled-coil structure. Terskikh *et al* teach that various forms of this domain can be readily produced in *E. coli* and easily purified to near homogeneity under nondenaturing conditions. "These properties, taken together with a remarkable solubility in salt-free water (up to 20 mg/ml) and thermostability, make the COMP assembly domain an ideal pentamerization tool for protein engineering...thus....bypasses the difficulties previously encountered during the expression of oligomeric forms of relatively complex proteins...". Terskikh *et al* teach that the fusion of the protein-COMP construct to other different relevant polypeptides such as an FcR binding domain, would provide new functional properties to this molecule in addition to the multivalent high avidity binding (especially abstract, Introduction, first paragraph at column 1 on page 1664, discussion section).

Muller *et al* teach that chimeric multimers made by genetic fusions to heterologous oligomerization domains can be constructed with coiled coils that act as versatile fusion partners, having small domains with predictable quaternary structure and adjustable stability (especially first paragraph). Muller *et al* teach that the best-characterized pentamer occurs in COMP (especially page 264, last sentence at the end of the first full paragraph). Muller *et al* teach using coiled coils to generate chimeric proteins with higher avidity (especially paragraph spanning pages 267-269). Muller *et al* teach that the coiled coil can be genetically fused to the protein of interest via a flexible linker (especially first sentence on page 269). Muller *et al* teach adding fluorescent labels to the multimers, and use of the multimers for numerous biochemical, genetic, diagnostic and therapeutic applications (especially page 281 at the last two paragraphs).

Efimov *et al* (1994) teach that amino acid residues 20-83 of COMP protein can be over-expressed in *E. coli* and purified under non-denaturing conditions. Efimov *et al* teach that this fragment forms pentamers similar to the assembly domain of the native protein, and its five chains can be covalently linked *in vitro* by oxidation of cysteines 68 and 71. Efimov *et al* teach that this fragment adopts a predominantly α-helical structure as judged by circular dichroism spectroscopy (especially abstract).

Efimov *et al* (1996) teach that COMP is a pentameric glycoprotein and that self-association of COMP is achieved through the formation of a five-stranded α-helical bundle that involves amino acid residues 20-83, and the further stabilization by interchain disulfide bonds between cysteines 68 and 71. Efimov *et al* (1996) teach that COMP assembly domain has features of a coiled-coil (especially abstract and introduction section).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have substituted the coiled-coil domain disclosed by US 2005/0003431 A1 with the coiled-coil COMP assembly domain taught by Terskikh *et al*, Muller *et al*, Efimov *et al* (1994) and Efimov *et al* (1996).

One of ordinary skill in the art at the time the invention was made would have been motivated to do this because US 2005/0003431 A1 discloses such oligomeric complexes containing coiled-coil domains and the advantages of using them to increase avidity of MHC complexes, Terskikh *et al* teach that the COMP assembly domain spontaneously forms a five-stranded α helical bundle, the highest oligomerization state know for a compact coiled-coil structure, and this domain can be readily produced in *E. coli* and easily purified to near homogeneity under non-denaturing conditions, and use of such domain can bypass problems encountered in the expression of oligomerized forms of relatively complex proteins, Muller *et al* teach the versatility and stability of coiled-coil domains for oligomerizing proteins, the advantage of increased avidity that their use provides, and their use in various diagnostic and therapeutic applications, Efimov *et al* (1994) teach that amino acid residues 20-83 of COMP protein can be over-expressed in *E. coli* and purified under non-denaturing conditions, and Efimov *et al* (1996) teach the location of the COMP assembly domain, that it spontaneously forms a pentameric structure and is a coiled-coil domain.

16. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

17. Claims 1-12 and 20 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-21 and 29 of copending Application No. 10/770,140. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of '140 are encompassed by the instant claims.

18. Claims 1-12 and 20 are directed to an invention not patentably distinct from claims 1-21 and 29 of commonly assigned 10/770,140 as enunciated supra.

19. The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300). Commonly assigned 10/770,140, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

20. Claims 1-12 and 20 are rejected under 35 U.S.C. 102(e) as being anticipated by US 2005/0074848 A1 (publication of commonly assigned 10/770,140).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

US 2005/0074848 A1 discloses the oligomeric MHC complex and pharmaceutical composition thereof recited in the instant claims (see entire document, especially claims).

The instant claims "comprise" the recited components.

21. No claim is allowed.

22. The Examiner has not searched the UK 0219459.8 application because Applicant has not provided a certified copy. The Examiner has not searched PCT/EP03/09056 because Applicant has not provided a copy or made the corresponding WO publication number of record.

23. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware of in the specification.

24. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Marianne DiBrino whose telephone number is 571-272-0842. The Examiner can normally be reached on Monday, Tuesday, Thursday and Friday.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Christina Y. Chan, can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Marianne DiBrino

Marianne DiBrino, Ph.D.
Patent Examiner
Group 1640
Technology Center 1600
December 21, 2006

Christina Chan

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600